

Revised in  
PCT

44

CLAIMS:



1. A method for forming particles of a substance, the method comprising (a) co-introducing into a particle  
5 formation vessel, the temperature and pressure in which are controlled, a supercritical fluid; a solution or suspension of the substance in a first vehicle; and, separately from the solution or suspension, a second vehicle which is both substantially miscible with the  
10 first vehicle and substantially soluble in the supercritical fluid; and (b) using the supercritical fluid to disperse the solution or suspension and the second vehicle, and to extract the vehicles, substantially simultaneously and substantially immediately on  
15 introduction of the fluids into the particle formation vessel, wherein contact between the solution or suspension and the second vehicle occurs either substantially simultaneously with, or immediately before, dispersion of the solution or suspension and the second vehicle by the  
20 action of the supercritical fluid and extraction of the vehicles by the supercritical fluid.

2. A method according to claim 1, wherein the substance is soluble, or substantially soluble, only in solvents  
25 which are themselves substantially insoluble in the supercritical fluid, or is incompatible with a solvent which is soluble or substantially soluble in the supercritical fluid.

30 3. A method according to claim 1 or claim 2, wherein an

excess of the second vehicle over the first is achieved at their moment of contact, by means of appropriate flow rates for the two vehicles on their introduction into the particle formation vessel.

5

4. A method according to any one of the preceding claims, wherein the amount of the first vehicle used is less than or equal to about 30% of the total amount of the first and second vehicles used.

10

5. A method according to any one of the preceding claims, wherein the supercritical fluid contains one or more modifiers.

15

6. A method according to any one of the preceding claims, wherein one of the two vehicles contains functional groups that can hydrogen-bond or otherwise interact with functional groups contained in the other vehicle.

20

7. A method according to any one of the preceding claims, wherein the substance and the first vehicle are substantially polar, the second vehicle is substantially non-polar and both vehicles are substantially miscible in all proportions and substantially soluble in the supercritical fluid.

25

8. A method according to any one of claims 1-6, wherein the substance and the first vehicle are substantially non-polar, the second vehicle is substantially polar and both vehicles are substantially miscible in all proportions and substantially soluble in the supercritical fluid.

30

9. A method according to any one of the preceding claims wherein the substance is substantially insoluble in the

35

second vehicle.

10. A method according to claim 9, wherein the second vehicle contains a crystallisation seed, of an appropriate material which is insoluble in the second vehicle, to induce nucleation of the substance from which particles are to be formed, when the second vehicle comes into contact with the solution or suspension of the substance in the first vehicle.
11. A method according to claim 10, wherein the substance from which particles are to be formed is for use in or as a pharmaceutical, and the seed is or comprises a pharmaceutically acceptable carrier for the substance.
12. A method according to any one of the preceding claims, wherein the supercritical fluid, the solution or suspension and the second vehicle are co-introduced into the particle formation vessel by means of a nozzle having an outlet end communicating with the interior of the particle formation vessel, and two or more coaxial passages which terminate adjacent or substantially adjacent to one another at the outlet end, at least one of the passages serving to introduce a flow of the supercritical fluid into the particle formation vessel, at least one of the passages serving to introduce a flow of the solution or suspension of the substance in the first vehicle and at least one of the passages serving to introduce a flow of the second vehicle.
13. A method according to claim 12, wherein the nozzle is able to cause pre-filming of the solution or suspension and/or the second vehicle to occur, immediately prior to their dispersion by the supercritical fluid.

14. A method according to claim 12 or claim 13, wherein the solution or suspension of the substance in the first vehicle is introduced into the particle formation vessel through one passage of the nozzle, and the supercritical fluid and the second vehicle are introduced together through another passage of the nozzle, such that mixing of the two vehicles can occur simultaneously with their dispersion and extraction by the supercritical fluid.
15. A method according to claim 14, wherein the nozzle has at least three coaxial passages, the solution or suspension being introduced between an inner and an outer flow of the supercritical fluid/second vehicle mixture.
16. A method according to claim 12 or claim 13, wherein the nozzle has at least three coaxial passages, the outlet of at least one of the inner nozzle passages being located a small distance upstream (in use) of the outlet of one of its surrounding passages, and wherein the solution or suspension and the second vehicle are introduced through the inner passage and surrounding passage in question so as to allow, in use, a degree of mixing to occur, between the solution or suspension and the second vehicle, within the nozzle.
17. A method according to claim 16, wherein the nozzle has at least four coaxial passages, and wherein the solution or suspension and the second vehicle are introduced into the particle formation vessel between an inner and an outer flow of the supercritical fluid.
18. A method according to any one of the preceding claims, wherein one or more of the following conditions is varied in order to control the size and/or size distribution and/or shape and/or crystalline form of the

particles formed; the flow rate(s) of the supercritical fluid and/or the solution or suspension and/or the second vehicle; the relative amounts of the two vehicles; the concentration of the substance in the first vehicle; the  
5 temperature inside the particle formation vessel; and the pressure inside the particle formation vessel.

19. A method according to any one of the preceding claims, wherein the pressure inside the particle formation  
10 vessel is maintained substantially in excess of the critical pressure of the fluid used as the supercritical fluid, whilst the temperature inside the particle formation vessel is maintained at only slightly above the critical temperature for that fluid.

15 20. A method according to any one of the preceding claims, wherein the ratio of the solution/suspension flow rate, into the particle formation vessel, to that of the supercritical fluid is between 0.001 and 0.2.

20 21. A method according to any one of the preceding claims, which is carried out substantially continuously, as opposed to batch-wise.

25 22. A method for forming particles of a substance, the method being substantially as herein described with reference to the accompanying illustrative drawings.

23. Apparatus for use in carrying out a method according  
30 to any one of the preceding claims, the apparatus comprising a particle formation vessel; means for controlling the temperature in the vessel at a desired level; means for controlling the pressure in the vessel at a desired level; and means for the co-introduction, into  
35 the vessel, of the supercritical fluid, the solution or

suspension of the substance in the first vehicle, and the second vehicle, in such a way that contact between the solution or suspension and the second vehicle occurs either substantially simultaneously with, or immediately before, dispersion of the solution or suspension and the second vehicle by the action of the supercritical fluid and extraction of the vehicles by the supercritical fluid, and such that the dispersion and extraction occur substantially simultaneously and substantially immediately on introduction of the fluids into the particle formation vessel, wherein the means for the co-introduction of the fluids into the vessel comprises a nozzle having an outlet end communicating with the interior of the vessel, and at least three coaxial passages which terminate adjacent or substantially adjacent to one another at the outlet end, at least one of the passages serving to introduce a flow of the supercritical fluid into the vessel, at least one of the passages serving to introduce a flow of the solution or suspension and at least one of the passages serving to introduce a flow of the second vehicle, all fluid flows being in substantially coaxial directions, and wherein the outlet of at least one of the inner nozzle passages is located a small distance upstream (in use) of the outlet of one of its surrounding passages so as to allow, in use, a degree of mixing to occur within the nozzle, between the solution or suspension and the second vehicle, when the solution/suspension and the second vehicle are introduced through the inner passage and surrounding passage in question.

30

24 . Apparatus according to claim 23 , wherein the nozzle is able to cause pre-filming of the solution or suspension and/or the second vehicle to occur, immediately prior to their dispersion by the supercritical fluid.

35

25 Apparatus according to claim 23 or claim 24, wherein the nozzle has four coaxial passages.

26. Apparatus according to any one of claims 23-25 ,  
5 wherein the angle of taper of the outlet end of the nozzle, with respect to the main axis of the nozzle, is in the range of about 10° to about 60°.

27. Apparatus according to any one of claims 23-26 ,  
10 comprising more than one particle formation vessel and/or more than one means for collecting the particles formed, thereby allowing for the substantially continuous operation of the apparatus through switching from one particle formation vessel or collection means to another  
15 as required.

28. Apparatus according to any one of claims 23-27 and substantially as herein described with reference to the accompanying illustrative drawings.

20

29. A particulate product made using a method according to any one of claims 1-22 , and/or apparatus according to any one of claims 23-28 .

25

*add ci?*